US Army Medical Research and Materiel

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Live Vaccine Against Brucellosis

This invention provides a method for preparing live vaccines against brucellosis using two genetically defined attenuated rough vaccine strains, WRR51 and WRRP1. The vaccines are prepared by introducing a deletion in the *rfbU* gene (recently renamed *wboA*) of two strains of *Brucella melitensis* which results in attenuation of the strains, while retaining the desired immunogenicity to initiate a protective immunogenic response. Both strains have a lipopolysaccharide (LPS) defect and thus do not cause the seroconversion that complicates disease screening. The WRRP1 strain is a highly attenuated double deletion mutant that is unlikely to cause human disease.

Brucella infects a significant number of people and livestock in developing countries as well as wild and domestic animals in the U.S. *Brucella* is also a biowarfare threat to military personnel, as multiple antibiotic resistant strains of *Brucella* have been constructed. In man, brucellosis may be caused by exposure to numerous strains of *Brucella* which also infect farm animals and dogs. Symptoms include recurring fever, chills and anxiety. The disease is rarely fatal, but once well established is difficult to treat since the bacteria reside in the bone marrow.

Both deletion strains were tested in human macrophages [illegible] able to infect them, had reduced capacity to grow within host cells. When tested in a mouse model, the WRRP1 strain only survived in the spleen one week or less and the WRR51 strain survived for 8 weeks or less. In contrast to a fully virulent *Brucella* strain which survived for 12 weeks in high numbers when those mice were sacrificed. The invention could potentially be used to vaccinate animals, dairy workers, animal handlers, and military personnel.

Features and advantages:

- **Defined, non-reverting deletion mutations**
- **Did not cause seroconversion in vaccinated mice**
- **WRRP1 strain cleared from mouse spleen cells within one week of intraperitoneal injection**
- **Highly attenuated WRRP1 strain is likely to address FDA's live vaccine concerns**
- **Could combine with mutations in *Brucella* genes to improve safety**

Patent Status

Patent No.: 6,444,445
Issued: September 3, 2002
Available from: www.uspto.gov
Docket No.: WRAIR 97-13

Point of Contact

Dr. Paul C. Mele
Director, Office of Research and Technology Applications
USAMRMC, MCM-ZA-J
504 Scott St., Frederick, MD 21702-5012
E-mail: usamrmcorta@amedd.army.mil
Voice: 301-619-6664/2065/7219 Fax: 301-619-5034

KEYWORDS: brucellosis; vaccine; *Brucella*; attenuated; biodefense

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